CLAIMS:-

1. A method for determining or identifying a compound that modulates the function of a blood vessel in an isolated retina, wherein a change in the contractile state of a blood vessel in an isolated retina is determined in the presence of a test compound, said change indicating that the test compound modulates blood vessel function.

2. A method for determining or identifying a compound that modulates the contractile state of a blood vessel in an isolated retina comprising contacting an isolated retina with a test compound and determining a change in the contractile state of said blood vessel, wherein said change indicates that the compound modulates the contractile state of the blood vessel.

3. The method for determining or identifying a compound of claims 1 or 2, wherein the retina is a whole retina.

4. The method for determining or identifying a compound of any one of claims 1-3, wherein the isolated retina is in physical contact with a support.

5. The method for determining or identifying a compound of any one of claims 1-4, wherein, the isolated retina is fixed to a support.

6. The method for determining or identifying a compound of any one of claims 1-5, wherein the isolated retina is fixed to the support using an adhesive, or by virtue of a vacuum.

7. A method of identifying a compound that modulates the contractile state of a blood vessel in an isolated retina comprising:

(i) providing an isolated retina fixed to a support;

(ii) contacting a test compound with said isolated retina; and

(iii) determining a distortion in said blood vessel, wherein said distortion indicates that said compound modulates the contractile state of a blood vessel in an isolated retina.

8. The method of identifying a compound of claim 7, wherein the isolated retina is aligned to the interior surface of the posterior segment of an eye.

9. The method of identifying a compound of claim 8, wherein the posterior segment is fixed to the support.

10. The method of identifying a compound of claim 7, wherein the isolated retina is aligned to a non-naturally occurring or synthetic surface.

11. The method of identifying a compound of claim 10, wherein the non-naturally occurring or synthetic surface is fixed to the support.

12. The method of identifying a compound of claim 10, wherein the non-naturally occurring or synthetic surface is substantially concave.

13. The method of identifying a compound of claim 10, wherein the non-naturally occurring or synthetic surface is substantially level or planar.

14. The method of identifying a compound of claim 10, wherein the isolated retina is flat mounted onto a substantially level or planar surface.

15. The method of identifying a compound of claim 10, wherein the synthetic surface is constructed of glass.

16. The method of identifying a compound of claim 10, wherein the synthetic surface is constructed of a polymer material.

17. The method of identifying a compound of claim 10, wherein the synthetic surface is constructed of a mixture of glass and polymer material.

18. The method of identifying a compound of any one of claims 7-17, wherein the support is a surface, container or a housing.

19. The method of identifying a compound of claim 18, wherein the support is a container which is capable of containing solution.

20. The method of identifying a compound of claim 18, wherein the support is a Petri dish.

21. The method of identifying a compound of claims any one of 1-20, wherein the blood vessel contains blood.

22. The method of identifying a compound of claims 1-20, wherein the blood vessel contains a dye.

23. The method of identifying a compound of claim 22 wherein the dye is Evans Blue dye.

24. The method of identifying a compound of claims 22 or 23, wherein the dye is perfused into the blood vessel.

25. The method of identifying a compound of any one of claims 2-24, wherein said test compound is contacted with the vitreous side of the isolated retina.

26. The method of identifying a compound of any one of claims 2-24, wherein said test compound is contacted with the non-vitreous side of the isolated retina.

27. The method of identifying a compound of any one of claims 1-26, wherein said test compound is administered in droplet form.

28. The method of identifying a compound of any one of claims 1-26, wherein said test compound is administered in the form of drops, vapour, atomised drops, nanoparticles, microspheres, or a mixture thereof.

29. The method of identifying a compound of any one of claims 1-26, wherein said test compound is administered in a stream of solution.

30. The method of identifying a compound of any one of claims 1-26, wherein said test compound is administered by perfusion.

31. The method of identifying a compound of any one of claims 1-26, wherein the method comprises incubating the isolated retina in the presence of a test compound.

32. The method of identifying a compound of any one of claims 2-31, wherein the contractile state of the blood vessel is determined before the compound is contacted with the blood vessel.

33. The method of identifying a compound of any one of claims 1-32, wherein the contractile state of a blood vessel is determined visually.

34. The method of identifying a compound of any one of claims 1-33, wherein the contractile state of a blood vessel is detected using a microscope.

35. The method of identifying a compound of any one of claims 1-34, wherein the size, dimension or volume of the blood vessel is determined.

36. The method of identifying a compound of claim 7-35, wherein the distortion is a distortion of the thickness or diameter of said blood vessel.

37. The method of identifying a compound of claim 36, wherein the diameter is the cross-sectional diameter of the blood vessel.

38. The method of identifying a compound of claims 36 or 37, wherein the diameter of the blood vessel is measured in pixels or in microns.

39. The method of identifying a compound of claim 38, wherein the cross-sectional diameter of the blood vessel is measured in pixels.

40. The method of identifying a compound of any one of claims 1-39, wherein the method further comprises contacting the isolated retina with a second test compound.

41. The method of identifying a compound of any one of claims 7-39, wherein the method *further* comprises:

(i) optionally washing the isolated retina with a suitable buffer or aqueous solvent that is not damaging to the integrity of the retina or contractile function of the retinal blood vessels for a time and under conditions sufficient to remove the compound or reduce its activity to a level that does not affect blood vessel contraction;

(ii) optionally determining a distortion in the retinal blood vessel;

(iii) contacting the retinal blood vessel with a second test compound; and

(iv) determining a distortion in said retinal blood vessel,

wherein said distortion indicates that said compound modulates the contractile state of the retinal blood vessel.

42. The method of identifying a compound of claim 41, wherein the second compound is an antagonist of the first compound.

43. The method of identifying a compound of claim 41, wherein the second compound is a protagonist of the first compound.

44. The method of identifying a compound of any one of claims 1-41, wherein the method further comprises a competition type assay, wherein the method comprises contacting a competitive inhibitor compound with the retinal blood vessel either before or after the candidate compound is contacted with the retinal blood vessel.

45. A method for determining or identifying a compound that modulates pericyte function, wherein a change in the contractile state of a pericyte is determined in the presence of a test compound, said change indicating that the test compound modulates pericyte function.

46. A method for determining or identifying a compound that modulates the contractile state of a pericyte comprising contacting a pericyte with a test compound and determining a change in the contractile state of said pericyte, wherein said change indicates that the compound modulates the contractile state of the pericyte.

47. A method for determining or identifying a compound of claims 45 or 46, wherein the pericyte is in physical contact with a resilient support.

48 A method for determining or identifying a compound of any one of claims 45-47, wherein the contractile state of a pericyte is determined by the growth of a pericyte on a medium having a resilient or flexible support that is capable of being distorted when the pericyte is in contact therewith and capable of being distorted when the contractile state of the pericytes in contact therewith is modified.

49. A method of identifying a compound that modulates the contractile state of a pericyte comprising

(i) providing a pericyte cell in physical contact with a resilient support under conditions sufficient for a pericyte contraction to distort said resilient support;

(ii) contacting a test compound with said pericyte cell; and

(iii) determining a distortion in said resilient support,

wherein said distortion indicates that said compound modulates the contractile state of the pericyte.

50. The method of identifying a compound of claim 49, wherein the resilient support is a resilient sheet.

51. The method of identifying a compound of claim 49, wherein the resilient support is constructed of glass.

52. The method of identifying a compound of claim 49, wherein the resilient support is constructed of a polymeric material.

53. The method of identifying a compound of claim 52, wherein the resilient support is constructed of a cross-linked polymer.

54. The method of identifying a compound of claim 52, wherein the polymeric material comprises an elastic polymer or polymer film with elastic properties.

55. The method of identifying a compound of claim 52, wherein the polymeric material is a visco-elastic material.

56. The method of identifying a compound of claim 52, wherein the support is constructed from transparent material.

57. The method of identifying a compound of claim 52, wherein the support is constructed of a mixture of glass and polymeric materials.

58. The method of identifying a compound of claim 52, wherein the support comprises glass having a cross-linked polymer layer.

59. The method of identifying a compound of claim 52, wherein the support has a cross-linked silicone fluid layer.

60. The method of identifying a compound of claim 49, wherein the support is level or planar.

61. The method of identifying a compound of any one of claims 45-60, wherein the contractile state of a pericyte is determined visually.

62. The method of identifying a compound of any one of claims 45-61, wherein the size, dimension or volume of the pericyte is determined.

63. The method of identifying a compound of any one of claims 45-62, wherein the contractile state of a blood vessel is detected using a microscope.

64. The method of identifying a compound of claim 52, wherein the distortion of the polymer layer is visualised as elastic distortion or wrinkling of the support.

65. The method of identifying a compound of claim 64, wherein the contractility of said pericyte is determined by counting the number of wrinkles or distortions of the support.

66. The method of identifying a compound of any one of claims 45-64, wherein said test compound is administered in droplet form

67. The method of identifying a compound of claim 66 wherein wherein said test compound is administered in drops, vapour, atomised drops, nanoparticles, microsheres or mixture thereof.

68. The method of identifying a compound of any one of claims 45-65, wherein said test compound is administered in a stream of solution.

69. The method of identifying a compound of any one of claims 45-65, wherein said test compound is administered by perfusion.

70. The method of identifying a compound of any one of claims 45-65, wherein the method comprises incubating the isolated retina in the presence of a test compound.

71. The method of identifying a compound of any one of claims 45-65, wherein the contractile state of the pericyte is determined before the compound is contacted with the pericyte.

72. The method of identifying a compound of any one of claims 45-71, wherein the method *further* comprises:

(i) optionally washing the pericyte with a suitable buffer or aqueous solvent that is not damaging to the integrity or contractile function of the cell for a time and under conditions sufficient to remove the compound or reduce its activity to a level that does not affect pericyte contraction;

(ii) optionally determining a distortion in said resilient support;

(iii) contacting the pericyte with a second test compound; and

(iv) determining a distortion in said resilient support,

wherein said distortion indicates that said compound modulates the contractile state of the pericyte.

73. The method of identifying a compound of claim 72, wherein the second compound is an antagonist of the first compound.

74. The method of identifying a compound of claim 72, wherein the second compound is a protagonist of the first compound.

75. The method of identifying a compound of any of claims 45-74, wherein the method further comprises a competition type assay, wherein the method comprises contacting a competitive inhibitor compound with the pericyte cell either before or after the candidate compound is contacted with the cell.

76. A method of diagnosing impaired pericyte function in a subject comprising administering to the subject a pharmaceutically acceptable amount of a compound that modulates pericyte function under conditions sufficient to modify the contractile state of a pericyte and determining the change in the contractile state of the subject's pericytes, wherein said compound is identified by a method comprising determining a

change in the contractile state of a pericyte in the presence of said compound, and wherein said change is indicative that the compound modulates pericyte function.

77. The method of diagnosing impaired pericyte function of claim 76, wherein the change in the contractile state of the subject's retinal blood vessel is determined by a comparison with the change in contractile state of a retinal blood vessel of a healthy subject.

78. The method of diagnosing impaired pericyte function of claims 76 or 77, wherein said compound is identified by a method according to any one of claims 45-75.

79. A method of diagnosing impaired retinal blood vessel function in a subject comprising administering to the subject a pharmaceutically acceptable amount of a compound that modulates blood vessel function under conditions sufficient to modify the contractile state of a blood vessel, wherein said compound is identified by a method comprising determining a change in the contractile state of a blood vessel in an isolated retina in the presence of said compound, wherein said change is indicative that the compound modulates blood vessel function, and detecting a change in the contractile state of the subject's retinal blood vessels.

80. The method of diagnosing impaired retinal blood vessel function of claim 79, wherein the change in the contractile state of the subject's pericytes is determined by a comparison with the change in contractile state of a pericyte of a healthy subject.

81. A method of diagnosing impaired retinal blood vessel function in a subject, the method comprising:

(i) administering to the subject a pharmaceutically acceptable amount of a compound that modulates the contractile state of a blood vessel in an isolated retina wherein said compound is identified by a process comprising determining a change in the contractile state of a blood vessel in an isolated retina in the presence of said compound, wherein said change is indicative that the compound modulates retinal vessel function; and

(ii) detecting a distortion of a blood vessel in the retina of the subject,

wherein a slow or unsubstantial dilation or constriction of the retinal vessel indicates retinal vessel damage.

82. The method of diagnosing impaired retinal blood vessel function in a subject of claims 80 or 81, wherein said compound is identified by a method according to any one of claims 1-44.

83. A method of diagnosing impaired retinal blood vessel function in a subject, the method comprising:

(i) administering to the subject a pharmaceutically acceptable amount of a compound that modulates the contractile state of a pericyte wherein said compound is identified by a process comprising determining a change in the contractile state of a pericyte in the presence of said compound, wherein said change is indicative that the compound modulates pericyte function; and

(ii) detecting a distortion of a blood vessel of the subject,

wherein a slow or unsubstantial dilation or constriction of the retinal vessel indicates retinal vessel damage.

84. The method of diagnosing impaired retinal blood vessel function of any one of claims 81 - 83, wherein the blood vessel is a capillary.

85. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-84, wherein the change in the contractile state of the subject's capillaries is determined by a comparison with the change in contractile state of a retinal capillary of a healthy subject.

86. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-85, wherein the compound is administered using an invasive route.

87. The method of diagnosing impaired retinal blood vessel function of claim 86 wherein, the invasive route is retrobulbar.

88. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-85, wherein the compound is administered using a non-invasive route.

89. The method of diagnosing impaired retinal blood vessel function of claim 88, wherein the non-invasive route comprises iontophoresis.

90. The method of diagnosing impaired retinal blood vessel function of claim 88, wherein iontophoresis is applied to the cornea of an eye.

91. The method of diagnosing impaired retinal blood vessel function of claim 88, wherein the compound is administered in droplet form.

92. The method of diagnosing impaired retinal blood vessel function of claim 91, wherein the compound is administered as drops, vapour, atomised droplets, nanoparticles, microspheres or a mixture thereof.

93. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-92, wherein the method comprises contacting the subject's eye with an effective amount of at least one compound selected from the group consisting of: pituitary adenylate cyclase-activating polypeptide (PACAP), vasoactive intestinal polypeptide (VIP), a compound having activity on phospholipase C (PLC), a compound having activity on protein kinase A (PKA), a compound having activity on ion-channel hyperpolarisation channels, and a non-steroidal anti-inflammatory drug (NSAID), or a homologue analogue or derivative thereof.

94. The method of diagnosing impaired retinal blood vessel function of claim 93, wherein a NSAIDs is selected from the group consisting of aspirin, pyrazolones, fenamate, diflunisal, acetic acid derivatives, propionic acid derivatives, oxicams, fenamates such as mefenamic acid, meclofenamate, phenylbutazone, diflunisal, diclofenac, Voltaren, indomethacin, sulindac, N-phenylanthranilic acid, etodolac, ketorolac, nabumetone, tolmetin, ibuprofen, fenoprofen, flurbiprofen, carprofen, ketoprofen, naproxen, , piroxicam, indomethacin and flufenamic acid or a derivative thereof.

95. The method of diagnosing impaired retinal blood vessel function of claim 93, wherein the NSAID is N-phenylanthranilic acid or flufenamic acid or flurbiprofen.

96. The method of diagnosing impaired retinal blood vessel function of claim 95, wherein the NSAID is flurbiprofen in the R-isomer form, or S-isomer form.

97. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-96, wherein the size, dimension or volume of the blood vessel is determined.

98. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-96, wherein the change or distortion is detected visually.

99. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-98, wherein detecting the change or distortion of the subject's retinal blood vessels comprises using a microscope, ophthalmoscope or Fundus camera.

100. The method of diagnosing impaired retinal blood vessel function of any one of claims 79-99, wherein an image of the retina is recorded.

101. The method of diagnosing impaired retinal blood vessel function of any one of claims 81-100, wherein the distortion is a distortion of the thickness or diameter of said blood vessel.

102. The method of diagnosing impaired retinal blood vessel function of claim 101, wherein the diameter is the cross-sectional diameter of the blood vessel.

103. The method of diagnosing impaired retinal blood vessel function of any one of claims 97-102, wherein the dimension is measured in pixels or in microns.

104. Use of a compound that modulates retinal blood vessel function in the preparation of a medicament for the treatment of impaired retinal blood vessel function in a subject, said compound being identified by a method comprising determining or identifying a change in the contractile state of a blood vessel in an isolated retina in the presence of said compound, wherein said change is indicative that the compound modulates retinal blood vessel function.

105. The use according to claim 104, wherein said compound is identified by a method according to any one of claims 1-44.

106. Use of a compound that modulates pericyte function in the preparation of a medicament for the treatment of impaired pericyte function in a subject, said compound being identified by a method comprising determining a change in the contractile state of a pericyte in the presence of said compound, wherein said change is indicative that the compound modulates pericyte function.

107. Use of a compound according to claim 106, wherein said compound is identified by a method according to any one of claims 45-75.

108. A method of treating a subject having impaired pericyte function comprising administering to the subject an amount of a pharmaceutical composition comprising a compound that modulates pericyte function and a pharmaceutically acceptable carrier, diluent or excipient, wherein said compound is identified by a process comprising determining a change in the contractile state of a pericyte in the presence of said compound, wherein said change is indicative that the compound modulates pericyte function.

109. The method according to claim 108, wherein said compound is identified by a method according to any one of claims 45-75.

110. A method of treating a subject having impaired retinal blood vessel function comprising administering to the subject an amount of a pharmaceutical composition comprising a compound that modulates pericyte function and a pharmaceutically acceptable carrier, diluent or excipient, wherein said compound is identified by a process comprising determining a change in the contractile state of a pericyte in the presence of said compound, wherein said change is indicative that the compound modulates pericyte function.

111. The method of treating a subject according to claim 110, wherein said compound is identified by a method according to any one of claims 45-75.

112. A method of treating a subject having impaired retinal blood vessel function comprising administering to the subject an amount of a pharmaceutical composition comprising a compound that modulates retinal blood vessel function and a pharmaceutically acceptable carrier, diluent or excipient, wherein said compound is identified by a process comprising determining a change in the contractile state of a blood vessel in an isolated retina in the presence of said compound, wherein said change is indicative that the compound modulates retinal blood vessel function.

113. The method of treating a subject according to claim 112, wherein said compound is identified by a method according to any one of claims 1-44.

114. The method of diagnosing impaired retinal blood vessel function in a subject of any one of claims 76 - 103, in monitoring progression of treatment in said subject.

Dated this Sixth day of June 2002